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File 155:MEDLINE(R) 1966-2002/Apr W1
File 5:Biosis Previews(R) 1969-2002/Apr W1
(c) 2002 BIOSIS

Set	Items	Description
? s sparc and (antisens? or ribozym?)		
	918	SPARC
	32970	ANTISENS?
	5731	RIBOZYM?
S1	12	SPARC AND (ANTISENS? OR RIBOZYM?)
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...completed examining records		
S2	8	RD (unique items)

? t s2/3,ab/all

2/3,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12632130 21575718 PMID: 11719371
Combined genomic and **antisense** analysis reveals that the transcription factor Erg is implicated in endothelial cell differentiation.
McLaughlin F; Ludbrook V J; Cox J; von Carlowitz I; Brown S; Randi A M
Cell Biology, CardioVascular Systems, and Genomics Units, GlaxoSmithKline Medicines Research Centre, Stevenage, United Kingdom.
Blood (United States) Dec 1 2001, 98 (12) p3332-9, ISSN 0006-4971 Journal Code: 7603509
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
It has recently been shown that the transcription factor Erg, an Ets family member, drives constitutive expression of the intercellular adhesion molecule 2 (ICAM-2) in human umbilical vein endothelial cells (HUVECs) and that its expression is down-regulated by the pleiotropic cytokine tumor necrosis factor alpha (TNF-alpha). To identify other Erg target genes and to define its function in the endothelium, a combined approach of **antisense** oligonucleotides (GeneBloc) and differential gene expression was used. Treatment of HUVECs with Erg-specific GeneBloc for 24, 48, and 72 hours suppressed Erg mRNA and protein levels at all time points. Total RNA extracted from HUVECs treated with Erg-specific or control GeneBloc was analyzed for differences in gene expression using high-density, sequence-verified cDNA arrays containing 482 relevant genes. Inhibition of Erg expression resulted in decreased expression of ICAM-2, as predicted. Four more genes decreased in Erg-deficient HUVECs were the extracellular matrix proteins **SPARC** and thrombospondin, the adhesive glycoprotein von Willebrand factor, and the small GTPase RhoA. Each of these molecules has been directly or indirectly linked to angiogenesis because of its role in vascular remodeling, adhesion, or shape change. Therefore, the role of Erg in vascular remodeling was tested in an in vitro model, and the results showed that HUVECs treated with Erg GeneBloc had a decreased ability to form tubulelike structures when grown on Matrigel. These results suggest that Erg may be a mediator of the TNF-alpha effects on angiogenesis in vivo.

2/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09629917 98103635 PMID: 9443398
Hevin, an antiadhesive extracellular matrix protein, is down-regulated in metastatic prostate adenocarcinoma.
Nelson PS; Plymate SR; Wang K; True LD; Ware JL; Gan L; Liu AY; Hood L
Department of Molecular Biotechnology, University of Washington, Seattle 98195, USA.
Cancer research (UNITED STATES) Jan 15 1998, 58 (2) p232-6, ISSN 0008-5472 Journal Code: CNF
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Hevin, a gene closely related to the extracellular matrix protein **SPARC** , is an acidic cysteine-rich glycoprotein shown to be important for the adhesion and trafficking of cells through the endothelium. Through the use of differential display and differential EST analysis, we identified Hevin as a gene whose transcription is down-regulated in transformed prostate epithelial cell lines and metastatic prostate adenocarcinoma. These results were confirmed by comparing expression levels between normal and neoplastic human prostate tissues using Northern analysis. In situ hybridization with an 35S-labeled **antisense** riboprobe demonstrated the loss of Hevin expression in metastatic prostate carcinoma. The expression pattern of Hevin in transformed and metastatic epithelium may provide further insights into the complex cell adhesion events involved in the metastatic progression of prostate carcinoma.

2/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09257900 97170962 PMID: 9018235
Suppression of **SPARC** expression by **antisense** RNA abrogates the tumorigenicity of human melanoma cells.
Ledda MF; Adris S; Bravo AI; Kairiyama C; Bover L; Chernajovsky Y; Mordoh J; Podhajcer OL
Instituto de Investigaciones Bioquimicas, Fundacion Campomar, Buenos Aires, Argentina.
Nature medicine (UNITED STATES) Feb 1997, 3 (2) p171-6, ISSN 1078-8956 Journal Code: CG5
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Acquisition of invasive/metastatic potential is a key event in tumor progression. Cell surface glycoproteins and their respective matrix ligands have been implicated in this process. Recent evidence reveals that the secreted glycoprotein **SPARC** (secreted protein, acidic and rich in cysteine) is highly expressed in different malignant tissues. The present study reports that the suppression of **SPARC** expression by human melanoma cells using a **SPARC antisense** expression vector results in a significant decrease in the in vitro adhesive and invasive capacities of tumor cells, completely abolishing their in vivo tumorigenicity. This is the first evidence that **SPARC** plays a key role in human melanoma invasive-metastatic phenotype development.

2/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09049533 96341098 PMID: 8734932
The role of **SPARC** gene in tumorigenic capacity of human melanoma cells]

2/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09049533 96341098 PMID: 8734932
The role of **SPARC** gene in tumorigenic capacity of human melanoma cells]
Rol del gen **SPARC** en la capacidad tumorigenica de celulas de melanoma humano.
Ledda MF; Adris S; Bover L; Bravo AL; Mordoh J; Podhajcer OL
Instituto de Investigaciones Bioquimicas Luis Leloir, Fundacion Campoma, Buenos Aires, Argentina.
Medicina (ARGENTINA) 1996, 56 (1) p51-4, ISSN 0025-7680
Journal Code: MMM
Languages: SPANISH
Document type: Journal Article
Record type: Completed
Previous studies from our laboratory have demonstrated that human melanoma cell lines and tumors expressed high levels of the extracellular protein **SPARC** . In order to demonstrate its role in human melanoma progression, IIB-MEL-LES human melanoma cells were transfected with **SPARC** full length c-DNA in the **antisense** orientation. In vivo studies demonstrated that all the control mice injected with parental cells developed tumors, while none of the mice injected with cells obtained from three different clones with diminished levels of **SPARC** expression, developed tumors. These studies suggest that **SPARC** may play a key role in human melanoma progression.

? 3,AB 2 Item 2 from file: 155
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

10007682 96341098 PMID: 8734932
The role of **SPARC** gene in tumorigenic capacity of human melanoma cells.
Rol del gen **SPARC** en la capacidad tumorigenica de celulas de melanoma humano.
Ledda M F; Adris S; Bover L; Bravo A I; Mordoh J; Podhajcer O L
Instituto de Investigaciones Bioquimicas Luis Leloir, Fundacion Campoma, Buenos Aires, Argentina.
Medicina (ARGENTINA) **1996**, 56 (1) p51-4, ISSN 0025-7680 Journal Code: 1204271
Document type: Journal Article ; English Abstract
Languages: SPANISH
Main Citation Owner: NLM
Record type: Completed
Previous studies from our laboratory have demonstrated that human melanoma cell lines and tumors expressed high levels of the extracellular protein **SPARC** . In order to demonstrate its role in human melanoma progression, IIB-MEL-LES human melanoma cells were transfected with **SPARC** full length c-DNA in the **antisense** orientation. In vivo studies demonstrated that all the control mice injected with parental cells developed tumors, while none of the mice injected with cells obtained from three different clones with diminished levels of **SPARC** expression, developed tumors. These studies suggest that **SPARC** may play a key role in human melanoma progression.

3/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

09005587 96361504 PMID: 8717113
The impact of **osteonectin** for differential diagnosis of osteogenic bone tumors: an immunohistochemical and in situ hybridization approach.
Park Y K; Yang M H; Park H R
Department of Pathology, College of Medicine, Kyung Hee University Medical Center, Seoul, Korea.
Skeletal radiology (GERMANY) Jan **1996**, 25 (1) p13-7, ISSN 0364-2348 Journal Code: 7701953
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Thirty-three osteosarcomas at various grades of histologic differentiation, including chondroblastic, osteoblastic, and fibroblastic variants, were investigated immunohistochemically for evidence of **osteonectin** . Twenty-two cases of varying types of osteosarcoma were examined with in situ hybridization for mRNA expression of **osteonectin**. Immunohistochemically, **osteonectin** was present in all the osteosarcomas in this study. With in situ hybridization, 12 out of 22 osteosarcomas showed a positive signal. Two osteochondrosarcomas, seven chondrosarcomas, and one mesenchymal chondrosarcoma were also studied with regard to the localization of **osteonectin** , either immunohistochemically or by in situ hybridization. Immunohistochemically, **osteonectin** was present in all the chondroid lesions except for one osteochondroma. However, in situ hybridization of **osteonectin** mRNA was negative in all the chondroid lesions we studied. This study revealed that immunohistochemical localization of **osteonectin** is not useful in providing conclusive diagnosis of osteosarcoma. In situ hybridization of

osteonectin mRNA might be useful in differentiating osteosarcoma from nonosteogenic bone tumors.

3/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

08656929 96017858 PMID: 7556670
Extracellular matrix components in intestinal development.
Simon-Assmann P; Kedinger M; De Arcangelis A; Rousseau V; Simo P
INSERM U.381, Strasbourg, France.
Experientia (SWITZERLAND) Sep 29 **1995**, 51 (9-10) p883-900, ISSN 0014-4754 Journal Code: 0376547
Document type: Journal Article; Review; Review, Academic
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Intestinal morphogenesis and differentiation are dependent on heterotypic cell interactions between embryonic epithelial cells (endoderm) and stromal cells (mesenchyme). Extracellular matrix molecules represent attractive candidates for regulators of these interactions. The structural and functional diversity of the extracellular matrix as intestinal development proceeds is demonstrated by 1) spatio-temporal specific expression of the classically described constituents, 2) the finding of laminin and collagen IV variants, 3) changes in the ratio of individual constituent chains, and 4) a stage-specific regulation of basement membrane molecule production, in particular by glucocorticoids. The orientation/assembly of these extracellular matrix molecules could direct precise cellular functions through interactions via integrin molecules. The involvement of extracellular matrix, and in particular basement membrane molecules in heterotypic cell interactions leading to epithelial cell differentiation, has been highlighted by the use of experimental models such as cocultures, hybrid intestines and **antisense** approaches. These models allowed us to conclude that a correct elaboration and assembly of the basement membrane, following close contacts between epithelial and fibroblastic cells, is necessary for the expression of differentiation markers such as digestive enzymes.

3/3,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

07694146 93228971 PMID: 1299273
Overexpression of **SPARC** in stably transfected P9 cells mediates attachment and spreading in Ca(2+)-deficient medium.
Everitt E A; Sage E H
Department of Biological Structure, School of Medicine, University of Washington, Seattle 98195.
Biochemistry and cell biology = Biochimie et biologie cellulaire (CANADA) Dec **1992**, 70 (12) p1368-79, ISSN 0829-8211 Journal Code: 8606068
Contract/Grant No.: 5T32-GM07270; GM; NIGMS; GM-40711; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The Ca(2+)-binding protein **SPARC** is one of a group of proteins that function in vitro to promote the rounding of cells. To assess whether the modulation of cell shape by **SPARC** is affected by extracellular Ca2+, we used P9 cell lines that had been stably transfected with sense or **antisense** **SPARC** DNA. Sense-transfected (S) lines that overexpress **SPARC** are aggregated and rounded, whereas **antisense**

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Set Items Description
S1 2141 SPARC OR OSTEONECTIN
S2 9 S1 AND PY=1998 AND (ANTISENS? OR RIBOZYM?)
S3 7 RD (unique items)
? s s1 and (tumor or cancer) and treat?
2141 S1
1072008 TUMOR
810450 CANCER
3364196 TREAT?
S4 53 S1 AND (TUMOR OR CANCER) AND TREAT?
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...examined 50 records (50)
...completed examining records
S5 37 RD (unique items)
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PLEASE ENTER A COMMAND OR BE LOGGED OFF IN 5 MINUTES
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Set Items Description
S1 2141 SPARC OR OSTEONECTIN
S2 9 S1 AND PY=1998 AND (ANTISENS? OR RIBOZYM?)
S3 7 RD (unique items)
S4 53 S1 AND (TUMOR OR CANCER) AND TREAT?
S5 37 RD (unique items)
? t s5/3,ab/all

5/3,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

14379153 22387089 PMID: 12499280
SPARC is a key Schwannian-derived inhibitor controlling neuroblastoma **tumor** angiogenesis.
Chlenski Alexandre; Liu Shuqing; Crawford Susan E; Volpert Olga V; DeVries George H; Evangelista Amy; Yang Qiwei; Salwen Helen R; Farrer Robert; Bray James; Cohn Susan L; et al
The Robert H. Lurie Comprehensive Cancer Center, Northwestern University, Feinberg School of Medicine, Chicago, Illinois 60611, USA.
Cancer research (United States) Dec 15 2002, 62 (24) p7357-63, ISSN 0008-5472 Journal Code: 2984705R
Contract/Grant No.: 5P30CA60553; CA; NCI; +
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Neuroblastoma (NB), a common pediatric neoplasm, consists of two main cell populations: neuroblastic/ganglionic cells and Schwann cells. NB tumors with abundant Schwannian stroma display a more benign clinical behavior than stroma-poor tumors. Recent studies suggest that Schwann cells influence NB **tumor** growth via secreted factors that induce differentiation, suppress proliferation, and inhibit angiogenesis. Two angiogenesis inhibitors, pigment epithelium-derived factor and tissue inhibitor of metalloproteinase-2, have been detected in Schwann cell secretions. Here, we isolated another Schwann cell-derived secreted inhibitor of angiogenesis, a 43 kDa protein identified as **SPARC** (secreted protein acidic and rich in cysteine), an extracellular matrix protein. We found **SPARC** to be critical for the antiangiogenic phenotype of cultured Schwann cells. We also show that purified **SPARC** potently inhibits angiogenesis and significantly impairs NB **tumor** growth in vivo. **SPARC** may be an effective candidate for the **treatment** of children with clinically aggressive, Schwannian stroma poor NB tumors.

5/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

14285098 22388710 PMID: 12501936
Doxycycline-inducible expression of **SPARC Osteonectin** BM40 in MDA MB 231 human breast **cancer** cells results in growth inhibition.
Shanesuan Nirada; Sharp Julie A; Blick Tony; Price John T; Thompson Erik W; et al
IBCRC Breast Cancer Invasion and Metastasis Unit, St. Vincent's Institute of Medical Research Melbourne, Australia.
Breast cancer research and treatment (Netherlands) Sep 2002, 75 (1) p73-85, ISSN 0167-6806 Journal Code: 8111104
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
SPARC (secreted protein acidic and rich in cysteine)/BM40/ **Osteonectin** is a matricellular protein with multiple effects on cell behaviour. In vitro, its major known functions are anti-adhesive and anti-proliferative, and it is associated with tissue remodelling and **cancer** in vivo. **SPARC** is overexpressed in many cancers, including breast **cancer**, and the effects of **SPARC** seem to be cell type-specific. To study the effects of **SPARC** on breast **cancer**, we transfected **SPARC** into the MDA-MB-231 BAG, human breast **cancer** cell line using the Tet-On inducible system. By western analysis, we found low background levels in the MDA-MB-231 BAG and clone X parental cells, and prominent induction of **SPARC** protein expression after doxycycline **treatment** in **SPARC** transfected clones X5, X21, X24 and X75. Induction of **SPARC** expression did not affect cell morphology or adhesiveness to collagens type I and IV, but it slowed the rate of proliferation in adherent cultures. Cell cycle analysis showed that **SPARC** slowed the progression to S phase. Doxycycline induction of **SPARC** also slowed the rate of monolayer wound closure in the cultured wound healing assay. Thymidine inhibition of proliferation abrogated this effect, confirming that it was due to anti-proliferation rather than inhibition of migration. Consistent with this, we were unable to detect any differences in migration and Matrigel outgrowth analysis of doxycycline-stimulated cells. We conclude that **SPARC** is inhibitory to human breast **cancer** cell proliferation, and does not stimulate migration, in contrast to its stimulatory effects reported for melanoma (proliferation and migration) and glioma (migration) cells. Similar growth repression by **SPARC** has been reported for ovarian **cancer** cells, and this may be a common feature among carcinomas.

5/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

14174480 22327653 PMID: 12440771
Genes involved in breast **cancer** metastasis to bone.
Sloan E K I; Anderson R L; et al
Treschowthick Research Laboratories, Peter MacCallum Cancer Institute, Melbourne, VIC, Australia.
Cellular and molecular life sciences - CMLS (Switzerland) Sep 2002, 59 (9) p1491-502, ISSN 1420-682X Journal Code: 9705402
Contract/Grant No.: CA090291; CA; NCI; +
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Metastasis to bone occurs frequently in advanced breast **cancer** and is accompanied by debilitating skeletal complications. Current **treatments** are palliative and new therapies that specifically prevent the spread of breast **cancer** to bone are urgently required. While our understanding of interactions between breast **cancer** cells and bone cells has greatly improved, we still know little about the molecular determinants that regulate specific homing of breast **cancer** cells to the bone. In this review, we focus on genes that have been implicated in migration and adhesion of breast **cancer** cells to bone, as well as genes that promote **tumor** cell proliferation in the bone microenvironment. In addition, the review discusses new technologies, including better animal models, that will further assist with the identification of the molecular determinants of bone metastasis and will guide the development of new therapies.

5/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

13733136 22247431 PMID: 12360412
Comparison of gene expression profiling between malignant and normal plasma cells with oligonucleotide arrays.
De Vos John; Thykjaer Thomas; Tarte Karin; Ensslen Matthias; Raynaud Pierre; Requirand Guilhem; Pellet Florence; Pantesco Veronique; Reme Thierry; Jourdan Michel; Rossi Jean-Francois; Orntoft Torben; Klein Bernard
INSERM U475, CHU Montpellier, 34 000 France.
Oncogene (England) Oct 3 2002, 21 (44) p6848-57, ISSN 0950-9232 Journal Code: 8711562
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The DNA microarray technology enables the identification of the large number of genes involved in the complex deregulation of cell homeostasis taking place in **cancer** . Using Affymetrix microarrays, we have compared the gene expression profiles of highly purified malignant plasma cells from nine patients with multiple myeloma (MM) and eight myeloma cell lines to those of highly purified nonmalignant plasma cells (eight samples) obtained by in vitro differentiation of peripheral blood B cells. Two unsupervised clustering algorithms classified these 25 samples into two distinct clusters: a malignant plasma cell cluster and a normal plasma cell cluster. Two hundred and fifty genes were significantly up-regulated and 159 down-regulated in malignant plasma samples compared to normal plasma samples. For some of these genes, an overexpression or downregulation of the encoded protein was confirmed (cyclin D1, c-myc, BMI-1, cystatin c, **SPARC** , RB). Two genes overexpressed in myeloma cells (ABL and cystathionine beta synthase) code for enzymes that could be a therapeutic target with specific drugs. These data provide a new insight into the understanding of myeloma disease and prefigure that the development of DNA microarray could help to develop an 'a la carte' **treatment** in **cancer** disease.

5/3,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

13403961 21687110 PMID: 11829440
Effect of different Ti-6Al-4V surface **treatments** on osteoblasts behaviour.
Hu Ching Hsin; Pioletti Dominique P; Browne Martin; Gregson Peter J
Bone Biophysics Group, Orthopaedic Hospital, Lausanne, Switzerland.
Biomaterials England Mar 2002, 23 6 p1447-54, ISSN 0142-9612

Journal Code: 8100316
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The purpose of the present work was to examine the effect of different Ti 6Al 4V surface **treatments** on osteoblasts behaviour. Previous work in this laboratory has demonstrated that an ageing **treatment** reduces metal ion release from this alloy compared to standard passivation procedures. In this study, human osteosarcoma MG-63 were used in short term in vitro tests to assay for cell viability and cell proliferation at 12, 24 and 72 h while SaOS-2 were used in long-term in vitro tests to assay for **osteonectin**, osteopontin, osteocalcin gene expression, total protein amount (TP), alkaline phosphatase activity (ALP) and fibronectin production (FN) for 1-4 weeks. Epifluorescence microscopy was used to observe SaOS-2 cell morphology. After 24h, there was no difference in MG-63 cell viability proliferation or in SaOS-2 cell morphology between the different surface **treatments**. For the long-term tests, the aged Ti-6Al-4V induced significantly higher cell proliferation than the control Ti-6Al-4V at 72h. At week 1, no difference in the **osteonectin**, osteopontin, and osteocalcin gene expression was found between samples. The peak of ALP activity appeared earlier at week 2 for the control surface compared with the passivated and aged surfaces. The early increase in ALP activity for the control sample could be a compensatory effect of decreased osteoblasts proliferation. There was no difference in the expression of FN for the different surface **treatments**. Our present results showed that the different surface **treatments**, which induced different metal ion release kinetics and surface properties, influenced the cell proliferation and ALP activity of osteoblast cells. Aluminium ions release kinetics as well as presence of vanadium ions may play a major role in influencing the osteoblasts behaviour in the present study.

9/3,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

13247677 21845817 PMID: 11856647
2-methoxyestradiol induces interferon gene expression and apoptosis in osteosarcoma cells.
Maran A; Zhang M; Kennedy A M; Sibonga J D; Rickard D J; Spelsberg T C; Turner R T
Department of Orthopedics, Mayo Foundation, MN, Rochester 55905, USA. maran@mayo.edu
Bone (United States) Feb 2002, 30 (2) p393-8, ISSN 8756-3282
Journal Code: 8904048
Contract/Grant No.: AR45233; AR; NIAMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
2-Methoxyestradiol (2-ME), a naturally occurring mammalian metabolite of 17beta-estradiol, has been implicated as a physiological inhibitor of **tumor** cell proliferation. In this study, the effects of 2-ME on cultured osteosarcomatous cells were investigated. Dose dependent growth inhibition was observed in MG63 and TE85 human osteosarcoma cells exposed to 2-ME. The cell killing by 2-ME was ligand-specific; the immediate precursor (2-hydroxyestradiol), the parent compound (17beta estradiol), and the equivalent metabolite of estrone (2 methoxyestrone) exhibited less potency and efficacy. Furthermore, 2-ME was similarly effective at killing immortalized human fetal osteoblastic cells (hFOB) with and without estrogen receptor alpha and beta and rat osteosarcoma cells (ROS17/2.8). The cytotoxicity of 2-ME was selective to transformed and immortalized osteoblastic cells; 2-ME 2 microM had no effect on the proliferation of

primary cultures of human osteoblasts. Co-**treatment** with the potent estrogen receptor ligand, ICI-182,780, did not reduce 2-ME-induced osteosarcoma cell death, implying that this action is not mediated by conventional estrogen receptors. The expression levels of bone matrix protein genes, type I collagen and **osteonectin**, were transiently reduced after 2-ME **treatment**, suggesting that the surviving cells are capable of producing bone matrix. The 2-ME-mediated killing of osteosarcoma cells was due to the induction of apoptosis; **treatment** induced expression of interferon genes within 12 h and histological evidence of apoptosis within 48 h of 2-ME **treatment**. Thus, our results demonstrate that 2-ME is highly cytotoxic to osteosarcoma cells but not normal osteoclasts. These findings suggest that further study of 2-ME as a potential intervention for **treatment** of osteosarcoma is warranted.

5/3,AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

13151769 21864315 PMID: 11874716
Modulation of gene expression in human osteoblasts by targeting a distal promoter region of human estrogen receptor-alpha gene.
Lambertini E; Penolazzi L; Sollazzo V; Pezzetti F; de Mattei M; del Senno L; Traina G C; Piva R
Dipartimento di Biochimica e Biologia Molecolare, University of Ferrara, Via L. Borsari 46, 44100 Ferrara, Italy.
Journal of endocrinology (England) Mar 2002, 172 (3) p693-98, ISSN 0022-0795 Journal Code: 0375363
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Estrogen receptor (ER) alpha is expressed during osteoblast differentiation; however, both its functional role in bone metabolism and its involvement in osteoporotic pathogenesis caused by estrogen deficiency are not well understood. Loss of ER alpha gene expression could be one of the mechanisms leading to osteoporosis. Therefore, we investigated a possible modulation of ER alpha gene expression in a human osteoblastic cell line and in four primary osteoblast cultures by using a decoy strategy. Double stranded DNA molecules, mimicking a regulatory region of the ER alpha gene promoter (DNA-102) and acting as a 'silencer' in breast **cancer** cells, were introduced into osteoblasts as 'decoy' cis-elements to bind and functionally inactivate a putative negative transcription factor, and thus to induce ER alpha gene expression. We found that the DNA-102 molecule was able to specifically bind osteoblast nuclear proteins. Before decoy **treatment**, absence or variable low levels of ER alpha RNAs in the different cultures were detected. When the cells were transfected with the DNA-102 decoy, an increase in expression of ER alpha and osteoblastic markers, such as osteopontin, was observed, indicating a more differentiated osteoblastic phenotype both in the cell line and in primary cultures. These results showed that the DNA-102 sequence competes with endogenous specific negative transcription factors that may be critical for a decrease in or lack of ER alpha gene transcription. Therefore, osteoblastic transfection with the DNA-102 decoy molecule may be considered a tempting model in a putative therapeutic approach for those pathologies, such as osteoporosis, in which the decrease or loss of ER alpha expression plays a critical role in bone function.

5/3,AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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10632130 21575718 PMID: 11719371

Combined genomic and antisense analysis reveals that the transcription factor Erg is implicated in endothelial cell differentiation.
McLaughlin F; Ludbrook V J; Cox J; von Carlowitz I; Brown S; Randi A M
Cell Biology, CardioVascular Systems, and Genomics Units, GlaxoSmithKline Medicines Research Centre, Stevenage, United Kingdom.
Blood United States Dec 1 2001, 98 12 p3312-9, ISSN 0006-4971 Journal Code: 7603509
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
It has recently been shown that the transcription factor Erg, an Ets family member, drives constitutive expression of the intercellular adhesion molecule 2 (ICAM-2) in human umbilical vein endothelial cells (HUVECs) and that its expression is down-regulated by the pleiotropic cytokine **tumor** necrosis factor alpha (TNF-alpha). To identify other Erg target genes and to define its function in the endothelium, a combined approach of antisense oligonucleotides (GeneBloc) and differential gene expression was used. **Treatment** of HUVECs with Erg-specific GeneBloc for 24, 48, and 72 hours suppressed Erg mRNA and protein levels at all time points. Total RNA extracted from HUVECs **treated** with Erg-specific or control GeneBloc was analyzed for differences in gene expression using high-density, sequence-verified cDNA arrays containing 482 relevant genes. Inhibition of Erg expression resulted in decreased expression of ICAM-2, as predicted. Four more genes decreased in Erg-deficient HUVECs were the extracellular matrix proteins **SPARC** and thrombospondin, the adhesive glycoprotein von Willebrand factor, and the small GTPase RhoA. Each of these molecules has been directly or indirectly linked to angiogenesis because of its role in vascular remodeling, adhesion, or shape change. Therefore, the role of Erg in vascular remodeling was tested in an in vitro model, and the results showed that HUVECs **treated** with Erg GeneBloc had a decreased ability to form tubulelike structures when grown on Matrigel. These results suggest that Erg may be a mediator of the TNF-alpha effects on angiogenesis in vivo.

5/3,AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

11326768 21378017 PMID: 11435919
SPARC (secreted protein acidic and rich in cysteine) induces apoptosis in ovarian **cancer** cells.
Yiu G K; Chan W Y; Ng S W; Chan P S; Cheung K K; Berkowitz R S; Mok S C
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American journal of pathology (United States) Aug 2001, 159 (2) p609-22, ISSN 0002-9440 Journal Code: 0370502
Contract/Grant No.: CA83381; CA; NCI; CA69453; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Secreted protein acidic and rich in cysteine (**SPARC**) is an extracellular Ca(2+)-binding matricellular glycoprotein that associates with cell populations undergoing migration, morphogenesis, and differentiation. Studies on endothelial cells have established that its principal functions in vitro are counteradhesion and antiproliferation. The mechanism(s) underlying these antitumor effects is unknown. In this study, we showed that **SPARC** expression in ovarian **cancer** cells is inversely correlated with the degree of malignancy. The immunohistochemical data presented here confirmed the importance of diminished **SPARC** expression in ovarian **cancer** development. **Treating** human

ovarian surface epithelial cells and ovarian **cancer** cells with **SPARC** revealed that as **SPARC** inhibits the proliferation of both normal and **cancer** cells, it induces apoptosis only in **cancer** cells. This observation indicates that down-regulation of **SPARC** is essential for ovarian carcinogenesis as **cancer** cells become sensitized to the apoptotic activity of **SPARC** during malignant transformation. We also showed here the first direct evidence that putative **SPARC** receptors are present on ovarian epithelial cells. Their levels are higher in human ovarian surface epithelial cells than **cancer** cells. Binding of **SPARC** to its receptor is likely to trigger tissue-specific signaling pathways that mediate its **tumor** suppressing functions. Decrease in ligand-receptor interaction by the down-regulation of **SPARC** and/or its receptor is essential for ovarian carcinogenesis.

5/3,AB/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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11301354 21341706 PMID: 11448934
High expression of the Cap43 gene in infiltrating macrophages of human renal cell carcinomas.
Nishie A; Masuda K; Otsubo M; Migita T; Tsuneyoshi M; Konno K; Snuin T; Naito S; Ono M; Kuwano M
Departments of Medical Biochemistry, Graduate School of Medical Sciences, Kyushu University, Fukuoka 812-8582, Japan.
Clinical cancer research : an official journal of the American Association for Cancer Research (United States) Jul 2001, 7 (7) p2145-51, ISSN 1078-0432 Journal Code: 9502500
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We used suppression subtractive hybridization to identify highly expressed genes in the cancerous region of human renal cell carcinoma (RCC) compared with noncancerous tissue. Nine genes were identified to show increased expression in the cancerous region compared with the noncancerous region. The nine genes included thymosin beta4, secreted protein acidic and rich in cysteine (**SPARC**), Cap43, ceruloplasmin, serum amyloid A, osteopontin, heat shock protein 90 (HSP90), LOT1, and casein kinase I. Of these 9 genes, in situ hybridization with 10 clinical samples consistently showed a strong expression of Cap43 mRNA in infiltrating macrophages in RCCs, but not in **cancer** cells proliferating in an alveolar pattern. However, Cap43 mRNA was also apparently detected in epithelial cells of the renal proximal tubuli in noncancerous tissue. The higher expression of the Cap43 gene in the cancerous region of RCCs appears to depend on macrophage infiltration. Moreover, **treatment** with phorbol ester resulted in enhanced expression of the Cap43 gene in human monocytic cells in vitro. The expression of the Cap43 gene in infiltrating macrophages is discussed in association with the differentiated or activated status of monocyte/macrophage.

5/3,AB/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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11088539 21084498 PMID: 11216681
The effects of particulate wear debris, cytokines, and growth factors on the functions of MG-63 osteoblasts.
Vermes C; Chandrasekaran R; Jacobs J J; Galante J O; Roebuck K A; Glant T T
Department of Orthopedic Surgery, Rush Presbyterian-St. Luke's Medical Center, Chicago, Illinois 60612, USA.

Journal of bone and joint surgery. American volume United States Feb 2001, 83-A 2 pp11-11, ISSN 0021-9355 Journal Code: 0014030
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

BACKGROUND: Particle-challenged cells release cytokines, chemokines, and eicosanoids, which contribute to periprosthetic osteolysis. The particle-induced activation of macrophages and monocytes has been extensively studied, but only limited information is available on the response of osteoblasts to particulate wear debris. This study examines the effects of particulate wear debris, proinflammatory cytokines, and growth factors on osteoblast functions. METHODS: MG-63 osteoblasts were **treated** with metal particles (titanium, titanium alloy, and chromium orthophosphate) or polymeric particles (polyethylene and polystyrene) of phagocytosable sizes or were **treated** with exogenous cytokines and growth factors. The kinetics of particle phagocytosis and the number of engulfed particles were assessed with use of fluoresceinated particles. Cell proliferation was determined according to [3H]-thymidine incorporation, and cell viability was determined by either fluorescein diacetate uptake or trypan blue exclusion. Expressions of osteoblast-specific genes were quantified with Northern blot hybridization, and the secretions of osteoblast-specific proteins and cytokines were analyzed by enzyme-linked immunosorbent assays. RESULTS: MG-63 osteoblasts phagocytosed particles and became saturated after twenty-four hours. A maximum of forty to sixty particles per cell were phagocytosed. Each type of particle significantly suppressed procollagen alpha1[I] gene expression ($p<0.05$), whereas other osteoblast-specific genes (**osteonectin**, osteocalcin, and alkaline phosphatase) did not show significant changes. Particle-stimulated osteoblasts released interleukin-6 ($p<0.05$) and a smaller amount of transforming growth factor-beta1. Particles reduced cell proliferation in a dose-dependent manner without affecting cell viability ($p<0.05$). Exogenous **tumor** necrosis factor-alpha also enhanced the release of interleukin-6 ($p<0.01$) and transforming growth factor-beta1 ($p<0.05$), whereas the secretion of transforming growth factor-beta1 was increased by insulin-like growth factor-I and prostaglandin E2 as well. Insulin-like growth factor-I and transforming growth factor-beta1 significantly increased procollagen alpha1[I] gene expression in osteoblasts ($p<0.05$), while **tumor** necrosis factor-alpha and prostaglandin E2 significantly suppressed procollagen alpha1[I] gene expression ($p<0.01$). In contrast, neither exogenous nor endogenous interleukin-6 had any effect on other cytokine secretion, on proliferation, or on procollagen alpha1[I] gene expression. The transcription inhibitor actinomycin D reduced both procollagen alpha1[I] transcription and interleukin-6 production. Inhibitors of protein synthesis (cyclohexamide) and intracellular protein transport (brefeldin A and monensin) blocked the release of interleukin-6, but none of these compounds influenced the suppressive effect of titanium on procollagen alpha1[I] gene expression. CONCLUSIONS: MG-63 osteoblasts phagocytose particulate wear debris, and this process induces interleukin-6 production and suppresses type-I collagen synthesis. Osteoblast-derived interleukin-6 may induce osteoclast differentiation and/or activation, but the resorbed bone cannot be replaced by new bone because of diminished osteoblast function (reduced type-I collagen synthesis). Exogenous cytokines (**tumor** necrosis factor-alpha and interleukin-1beta), growth factors (insulin-like growth factor-I and transforming growth factor-beta1), and prostaglandin E2 can modify particulate-induced alterations of osteoblast functions.

10961325 20530427 PMID: 11076659

Gene expression profiles in thyroid carcinomas.
Takano T; Hasegawa Y; Matsuzuka F; Miyauchi A; Yoshida H; Higashiyama T; Kuma K; Amino N
Department of Laboratory Medicine, Osaka University Medical School, D2 1-2 Yamadaoka, Suita, Osaka, 565-0871, Japan.
British journal of cancer SCOTLAND Dec 2000, 83 11 p1485-90, ISSN 0007-0920 Journal Code: 0370635
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The gene expression profiles of human thyroid carcinomas were analysed by serial analysis of gene expression (SAGE) which allows quantitative and simultaneous analysis of a large number of transcripts. More than 29,000 transcripts derived from a normal thyroid tissue and four thyroid tumours were analysed. While extensive similarity was noted between the expression profiles of the normal thyroid tissue and three differentiated thyroid tumours, many transcripts, such as **osteonectin**, a-tubulin, glyceraldehyde-3-phosphate dehydrogenase, glutathione peroxidase, and thyroglobulin, were expressed at extremely different levels in differentiated and undifferentiated carcinomas. These data provide new information that might be used to identify genes useful for the diagnosis and **treatment** of thyroid carcinomas. Copyright 2000 **Cancer** Research Campaign.

5/3,AB/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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10797240 20329468 PMID: 10873067
Quantitative analysis of circulating **tumor** cells in peripheral blood of osteosarcoma patients using osteoblast-specific messenger RNA markers: a pilot study.
Wong I H; Chan A T; Johnson P J
Department of Anatomical and Cellular Pathology, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, New Territories, SAR. p781764@mailserv.cuhk.edu.hk
Clinical cancer research : an official journal of the American Association for Cancer Research (UNITED STATES) Jun 2000, 6 (6) p2183-6, ISSN 1078-0432 Journal Code: 9502500
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Metastasis is a major cause of mortality and morbidity in osteosarcoma (OS) patients. To monitor **tumor** dissemination, we assessed the circulating **tumor** burden in OS patients by semiquantitative reverse transcription-PCR using osteocalcin, **osteonectin**, osteopontin, and type I collagen (COLL) mRNAs as molecular markers. We distinguished levels of the mRNAs in peripheral blood between OS patients and healthy subjects using an OS-derived cell line (Saos-2) as a reference standard. We prospectively analyzed 40 peripheral blood samples from 11 OS patients at diagnosis and 29 healthy subjects. In all 29 (100%) healthy subjects, we detected osteocalcin, **osteonectin**, and osteopontin mRNAs that were most likely attributed to illegitimate transcription in normal hematopoietic cells. In contrast, we found low COLL mRNA levels in only 35% (10 of 29) of healthy subjects, but significantly higher COLL mRNA levels in 91% (10 of 11) of OS patients (P < 0.0001). The reverse transcription-PCR assay for COLL mRNA was sensitive down to the detection of 10 Saos-2 cells among 10(6) normal peripheral blood nucleated cells. The upper limit of COLL mRNA determined among the healthy subjects was found exceeded by six OS patients. The substantially elevated COLL mRNA levels in peripheral blood seemed to originate from circulating malignant cells in

these six OS patients, all of whom subsequently developed clinical metastases within 12 months of diagnosis ($P = 0.002$). Conversely, no metastases were detected in the remaining OS patients with normal COL1 mRNA levels. Quantification of COL1 mRNA may prove valuable for diagnosing OS micrometastasis and assessing prognosis.

5/3,AB/14 Item 14 from file: 155
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10785837 20320836 PMID: 10861485
Targeting angiogenesis inhibits **tumor** infiltration and expression of the pro-invasive protein **SPARC**.
Vajkoczy P; Menger M D; Goldbrunner R; Ge S; Fong T A; Vollmar B; Schilling L; Ullrich A; Hirth K P; Tonn J C; Schmiedek P; Rempel S A
Department of Neurosurgery, Klinikum Mannheim, University of Heidelberg, Mannheim, Germany. peter.vajkoczy@nch.ma.uni-heidelberg.de
International journal of cancer. Journal international du cancer (UNITED STATES) Jul 15 2000, 87 (2) p261-8, ISSN 0020-7136 Journal Code: 0042124
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The solid growth of high-grade glioma appears to be critically dependent on **tumor** angiogenesis. It remains unknown, however, whether the diffuse infiltration of glioma cells into healthy adjacent tissue is also dependent on the formation of new **tumor** vessels. Here, we analyze the relationship between **tumor** angiogenesis and **tumor** cell infiltration in an experimental glioma model. C6 cells were implanted into the dorsal skinfold chamber of nude mice, and **tumor** angiogenesis was monitored by intravital fluorescence videomicroscopy. Glioma infiltration was assessed by the extent of **tumor** cell invasion into the adjacent chamber tissue and by expression of **SPARC**, a cellular marker of glioma invasiveness. To test the hypothesis that glioma angiogenesis and glioma infiltration are codependent, we assessed **tumor** infiltration in both the presence and the absence of the angiogenesis inhibitor SU5416. SU5416 is a selective inhibitor of the VEGF/Flk-1 signal-transduction pathway, a critical pathway implicated in angiogenesis. Control tumors demonstrated both high angiogenic activity and **tumor** cell invasion accompanied by strong expression of **SPARC** in invading **tumor** cells at the **tumor**-host tissue border. SU5416-**treated** tumors demonstrated reduced vascular density and vascular surface in the **tumor** periphery accompanied by marked inhibition of glioma invasion and decreased **SPARC** expression. A direct effect of SU5416 on glioma cell motility and invasiveness was excluded by in vitro migration and invasion assays. These results suggest a crucial role for glioma-induced angiogenesis as a prerequisite for diffuse **tumor** invasion and a possible therapeutic role for anti-angiogenic compounds as inhibitors of both solid and diffuse infiltrative **tumor** growth. Copyright 2000 Wiley-Liss, Inc.

5/3,AB/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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10623006 20166410 PMID: 10703670
Downregulation of **SPARC** expression is mediated by nitric oxide in rat mesangial cells and during endotoxemia in the rat.
Walpen S; Beck K F; Eberhardt W; Apel M; Chatterjee P K; Wray G M; Thiemermann C; Pfeilschifter J
Zentrum der Pharmakologie, Klinikum der Johann Wolfgang

Goethe Universitat, Frankfurt am Main, Germany.
Journal of the American Society of Nephrology : JASN UNITED STATES
Mar 2000, 11 3 p468-76, ISSN 1046-6673 Journal Code: 9013836
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Nitric oxide NO has been implicated in several forms of glomerulonephritis. In this study, a low stringency reversed transcription PCR protocol was used to evaluate the action of NO on the mRNA expression pattern in rat mesangial cells MC . To mimic the state of glomerular inflammation, MC were stimulated by exposure to the cytokines interleukin-1beta and **tumor** necrosis factor-alpha into producing high levels of NO via expression of inducible nitric oxide synthase NOS . To detect NO-mediated effects, the resulting expression pattern was compared to that of MC stimulated by the cytokines in the presence of the NOS inhibitor N(G)-monomethyl-L-arginine L-NMMA . Computer analysis of a differentially expressed cDNA fragment resulted in a 100% homology to the recently characterized mRNA of **SPARC** (secreted protein acidic and rich in cysteine). Further characterization of **SPARC** regulation revealed a cytokine- and cAMP-dependent decrease in **SPARC** mRNA and protein levels. Blocking NO formation by L-NMMA reversed the effects of cytokines and cAMP on **SPARC** expression, suggesting an NO-mediated mechanism. The NO donors S-nitroso-N-acetyl-penicillamine and diethylenetriamine/NO further reduced **SPARC** expression in cytokine-**treated** MC as well as in controls. Moreover, downregulation of **SPARC** mRNA and protein expression in whole kidneys obtained from rats **treated** with endotoxin was observed. This downregulation of **SPARC** was reversed by **treatment** with L-N6-1 (iminoethyl) lysine dihydrochloride, a potent and highly selective inhibitor of inducible NOS. These data characterize **SPARC** as an NO-regulated gene. This observation may be important in the context of tissue remodeling in chronic inflammatory kidney diseases.

5/3,AB/16 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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10220795 99218563 PMID: 10200452
Differentially expressed genes in C6.9 glioma cells during vitamin D-induced cell death program.
Baudet C; Perret E; Delpech B; Kagnad M; Brachet P; Wion D; Caput D
INSERM U 298, Centre Hospitalier Universitaire, Angers, 49033 Angers Cedex, France.
Cell death and differentiation (ENGLAND) Jan 1998, 5 (1) p116-25, ISSN 1350-9047 Journal Code: 9437445
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
C6.9 rat glioma cells undergo a cell death program when exposed to 1, 25-dihydroxyvitamin D3 (1,25-D3). As a global analytical approach, we have investigated gene expression in C6.9 engaged in this cell death program using differential screening of a rat brain cDNA library with probes derived from control and 1,25-D3-**treated** cells. Using this methodology we report the isolation of 61 differentially expressed cDNAs. Forty-seven cDNAs correspond to genes already characterized in rat cells or tissues. Seven cDNAs are homologous to yeast, mouse or human genes and seven are not related to known genes. Some of the characterized genes have been reported to be differentially expressed following induction of programmed cell death. These include PMP22/gas3, MBP and beta tubulin. For the first time, we also show a cell death program induced up regulation of the c-myc associated primary response gene CPP, and of the proteasome PN3

subunit and TCTP mortalin genes. Another interesting feature of this 1,25-D3 induced cell death program is the down regulated expression of transcripts for the microtubule motor dynein heavy chain MAP 1C and of the calcium binding S100beta protein. Finally 15 upregulated cDNAs encode ribosomal proteins suggesting a possible involvement of the translational apparatus in this cell program. Alternatively, these ribosomal protein genes could be up-regulated in response to altered rates of cellular metabolism, as has been demonstrated for most of the other isolated genes which encode proteins involved in metabolic pathways. Thus, this study presents to our knowledge the first characterization of genes which are differentially expressed during a cell death program induced by 1, 25-D3. Therefore, this data provides new information on the fundamental mechanisms which participate in the antineoplastic effects of 1,25-D3 and on the machinery of a cell death program in a glioma cell line.

5/3,AB/17 (Item 17 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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10050296 99017532 PMID: 9802946
Effects of ethanol on gene expression in rat bone: transient dose-dependent changes in mRNA levels for matrix proteins, skeletal growth factors, and cytokines are followed by reductions in bone formation.
Turner R T; Wronski T J; Zhang M; Kidder L S; Bloomfield S A; Sibonga J D
Department of Orthopedics, Mayo Clinic, Rochester, Minnesota 55905, USA.
Alcoholism, clinical and experimental research (UNITED STATES) Oct 1998, 22 (7) p1591-9, ISSN 0145-6008 Journal Code: 7707242
Contract/Grant No.: AA11140; AA; NIAAA
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Several studies were performed in female rats to determine dose and time course changes in mRNA levels for matrix proteins in bone after a single administration of ethanol. As expected, dose-dependent transient increases in blood ethanol were measured. Additionally, there was mild hypocalcemia with no change in immunoreactive parathyroid hormone. Coordinated dose-dependent increases in mRNA for type 1 collagen, **osteonectin**, and osteocalcin were noted in the proximal tibial metaphysis 6 hr after ethanol was given, with the peak values occurring at a dose of 1.2 g/kg (0.4 ml). Similar increases in mRNA levels for matrix proteins were noted in lumbar vertebrae after ethanol **treatment**. The changes were specific for bone; ethanol had no effect on mRNA levels for matrix proteins in the uterus or liver, although the mRNA concentrations tended to be reduced in uterus. Message levels for several cytokines implicated in the regulation of bone turnover were also assayed; mRNA levels for transforming growth factor-beta1, transforming growth factor-beta2, interferon-gamma, and interleukin-6 were unchanged at doses ranging from 0.14 to 1.7 g/kg. At the highest dose of ethanol, the mRNA level for **tumor** necrosis factor-alpha was elevated while the level for insulin-like growth factor-1 was reduced. The time course effects of ethanol (0.4 ml dose) were determined in a separate experiment. Ethanol resulted in a transient increase in mRNA levels for the three bone matrix proteins assayed. However, matrix protein synthesis, as determined by incorporation of 3H-proline into the proximal tibial metaphysis, was not changed after 6 hr. The changes in mRNA levels for the matrix proteins were preceded by brief, transient decreases in mRNA levels for interleukin-1beta, interferon-gamma, and migration inhibitory factor, and followed by a more prolonged decrease in the mRNA level for insulin-like growth factor-1. A subsequent study was performed to determine the effects of repetitive daily **treatment** with ethanol on rat bone. After 7 days, there were highly significant decreases in the mRNA level for type 1 collagen, as well as decreased bone formation. These results suggest that ethanol may alter bone metabolism by disturbing

signal transduction pathways that regulate the expression of genes for bone matrix proteins, skeletal growth factors, and cytokines.

5/3,AB/18 Item 18 from file: 155
DIALOG(R)File 155:MEDLINE(R)
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09563985 97463900 PMID: 9322601
Osteocalcin and **osteonectin** immunoreactivity in the diagnosis of osteosarcoma.
Fanburg J C; Rosenberg A E; Weaver D L; Leslie K O; Mann K G; Taatjes D J ; Tracy R P
Department of Soft Tissue Pathology, Armed Forces Institute of Pathology, Washington, DC 20306-6000, USA.
American journal of clinical pathology (UNITED STATES) Oct 1997, 108 (4) p464-73, ISSN 0002-9173 Journal Code: 0370470
Contract/Grant No.: AG-08777; AG; NIA
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Osteosarcomas (OSAs) can be difficult to distinguish histologically from tumors with significantly different biologic potentials and **treatment** protocols. The correct diagnosis of OSA relies on identification of malignant osteoblasts that are capable of producing neoplastic bone. To determine the use of immunohistochemistry for the diagnosis of OSA, 106 tumors from the Massachusetts General Hospital and the University of Vermont were immunostained with monoclonal antiosteocalcin (OC) and antiosteonectin (ON) antibodies. They included 42 OSAs, 25 non-bone-forming sarcomas, 24 other malignant tumors including lymphomas, carcinomas, and melanomas, and 15 benign bone tumors. Cytoplasmic staining with OC showed 70% sensitivity and 100% specificity, while staining with ON showed 90% sensitivity and 54% specificity for bone-forming tumors, consistently staining cell types other than osteoblasts. Of the OSAs, 83% demonstrated matrix staining with one or both antibodies, whereas dense collagen was negative for both antibodies in all tumors. We conclude that **tumor** cell cytoplasmic staining with monoclonal OC may be helpful in distinguishing OSAs from other malignancies, and staining of extracellular matrix for OC and ON antibodies concurrently may help distinguish bone matrix from dense collagen.

5/3,AB/19 (Item 19 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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09381923 97293065 PMID: 9149118
Emergence of osteoblast-like cells in a neoplastic human salivary **cancer** cell line after **treatment** with 22-oxa-1alpha, 25-dihydroxyvitamin D3.
Sato M; Iga H; Yoshioka N; Fukui K; Kawamata H; Yoshida H; Hirota S; Kitamura Y
Second Department of Oral and Maxillofacial Surgery, Tokushima University School of Dentistry, Kuramoto-cho, Japan.
Cancer letters (IRELAND) May 19 1997, 115 (2) p149-60, ISSN 0304-3835 Journal Code: 7600053
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
A neoplastic clonal cell line, which was prepared by 5 azacytidine **treatment** of a neoplastic human salivary intercalated duct cell line, was cultivated in the presence of 22-oxa-1alpha, 25-dihydroxyvitamin D3 and

3 mM beta-glycerophosphate. Major alterations, such as expression of type I collagen and alkaline phosphatase as well as of human osteopontin and **osteonectin**, were observed in these cells with a phenotype similar to osteoblasts. In addition, formation of bone nodule was observed in the cultured cells. The tumors produced by transplantation into nude mice of the clonal cells were **treated** with 22-oxa-1alpha, 25-dihydroxyvitamin D3 and examined for **tumor** growth and morphology. Consequently, growth of the **treated tumor** was significantly suppressed. Moreover, it was found that bone formation was induced in the **treated tumor**, in which the **tumor** cells around bone formation expressed human osteopontin and **osteonectin** mRNA as could be detected by in situ hybridization. The above findings indicate that the emergence of osteoclast-like cells in the human salivary **cancer** cells occurs in the presence of 22-oxa-1alpha, 25-dihydroxyvitamin D3 and beta-glycerophosphate.

5/3,AB/20 (Item 20 from file: 155)
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09306948 97193458 PMID: 9041049
Establishment and characterization of conditionally immortalized stromal cell lines from a temperature-sensitive T-Ag transgenic mouse.
Feuerbach D; Loetscher E; Buerki K; Sampath T K; Feyen J H
Department of Arthritis and Bone Metabolism, Novartis Pharma, Basel, Switzerland.
Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research (UNITED STATES) Feb 1997, 12 (2) p179-90, ISSN 0884-0431 Journal Code: 8610640
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We established bone marrow stromal cell lines from a transgenic mouse that harbors a temperature-sensitive mutant of the simian virus 40-derived large T-antigen under the control of a major histocompatibility complex (MHC) I promotor. These cell lines were screened for their ability to induce the formation of osteoclasts in a spleen cell/stromal cell coculture system. By means of this screen, five clones, referred to as marine bone marrow stromal clone 1 (mBMS-B1) mBMS-B2, mBMS-B14, mBMS-B18, and mBMS-B21, were selected for detailed characterization. Cell growth depends on culture conditions, i.e., cells grow at 33 degrees C in the presence of murine interferon-gamma, whereas cell proliferation ceases at 39 degrees C. The phenotype of the cells is also correlated with the culture conditions because the osteoclast inductive capacity is only seen at 39 degrees C, indicating that the cells undergo differentiation when the transforming agent is inactivated. These conditionally immortalized stromal cells can be induced to express a variety of markers that are typical for mature osteoblasts, e.g., alkaline phosphatase activity and expression of functional parathyroid hormone receptor after stimulation with soluble osteogenic protein 1 (sOP-1). mRNA analysis revealed the expression and regulation of osteopontin, **osteonectin**, and collagen alpha 1(I) as well as the inducibility of osteocalcin upon **treatment** with sOP-1. The cells have the potential to form mineralized nodules in supplemented medium. We observed expression of vascular cell adhesion molecule-1, which is stimulated upon **treatment** of the cells with 1 alpha,25-dihydroxycholecalciferol after 4 days, indicating the presence of the receptor for this steroid. These cell lines represent a model to study mechanisms and factors involved in osteoblast differentiation.

5/3,AB/21 (Item 21 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

96183485 97149412 PMID: 8894142
Phase-Dependent effects of transforming growth factor beta 1 on osteoblastic markers of human osteoblastic cell line SV-HFO during mineralization.
Iba H; Sawada N; Nuka S; Chiba H; Obata H; Isomura H; Satoh M; Ishii S; Mori M
Department of Pathology, Sapporo Medical University School of Medicine, Japan.
Bone UNITED STATES Oct 1996, 19 (4) p363-9, ISSN 8756-3282 Journal Code: 8804048
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
A human osteoblastic cell line (SV-HFO) established in our laboratory expresses osteoblastic markers, including mineralization in vitro, in response to differentiation-inducing agents such as dexamethasone. In this study, we examined the effects of transforming growth factor beta 1 (TGF-beta 1) on the mineralization of SV-HFO cells and show that TGF-beta 1 inhibited the mineralization of the cells via down-regulation of tetranectin and alkaline phosphatase without influencing other osteoblastic markers. To examine precisely the effects of TGF-beta 1 on the process of mineralization, we tentatively divided the whole process of mineralization into four phases: induced ALP activity (days 0-5), maximal ALP activity (days 5-10), early mineralization (days 10-15), and progressive mineralization (days 15-20). These inhibitory effects of TGF-beta 1 on the expression of tetranectin and alkaline phosphatase, like that on mineralization, were observed only when TGF-beta 1 was applied in the early phase of the process of mineralization. On the other hand, the other osteoblastic markers were not influenced by **treatment** with TGF-beta 1. These results suggest that TGF-beta 1 may inhibit mineralization of osteoblasts by the downregulation of tetranectin and alkaline phosphatase expression in the early phase. Thus, TGF-beta 1 has phase-dependent effects on a human osteoblastic cell line during the process of mineralization.

09515750 95274416 PMID: 7754797
Development and characterization of a conditionally immortalized human fetal osteoblastic cell line.
Harris S A; Enger R J; Riggs B L; Spelsberg T C
Department of Biochemistry and Molecular Biology, Mayo Clinic, Rochester, Minnesota, USA.
Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research (UNITED STATES) Feb 1995, 10 (2) p178-86, ISSN 0884-0431 Journal Code: 8610640
Contract/Grant No.: AR41652; AR; NIAMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We report the establishment of a human fetal osteoblast cell line derived from biopsies obtained from a spontaneous miscarriage. Primary cultures isolated from fetal tissue were transfected with a gene coding for a temperature-sensitive mutant (tsA58) of SV40 large T antigen along with a gene coding for neomycin (G418) resistance. Individual neomycin resistant colonies were screened for alkaline phosphatase (AP) specific staining. The clone with the highest AP level, hFOB 1.19, was examined further for other osteoblast phenotypic markers. Incubation of hFOB cells at the permissive

temperature 33.5 degrees C resulted in rapid cell division, whereas little or no cell division occurred at the restrictive temperature 39.5 degrees C . Both AP activity and osteocalcin OC secretion increased in a dose dependent manner following dihydroxyvitamin D3 1,25-D3 **treatment** when cultured at either temperature. However, AP and 1,25-D3-induced OC levels were elevated in confluent hFOB cells cultured at 39.5 degrees C compared with 33.5 degrees C. **Treatment** of hFOB cells with 1-34 parathyroid hormone PTH resulted in an increase in cAMP levels. Upon reaching confluence, hFOB cultures went through programmed differentiation and formed mineralized nodules as observed by von Kossa staining. Further, immunostaining of postconfluent, differentiated hFOB cells showed that high levels of osteopontin, **osteonectin**, bone sialoprotein, and type I collagen were expressed. Therefore, the clonal cell line hFOB 1.19 provides a homogeneous, rapidly proliferating model system to study certain stages of human osteoblast differentiation.

5/3,AB/23 (Item 23 from file: 155)
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08387287 95152796 PMID: 7849963
The use of Imagent BP as a blood pool contrast agent to visualize and quantitate liver **tumor** burden.
Steinbach B C; Baker K G; Lim G L; Mattrey R F; Arellano R S
Department of Radiology, University of California, San Diego.
Artificial cells, blood substitutes, and immobilization biotechnology (UNITED STATES) 1994, 22 (4) p1501-9, ISSN 1073-1199 Journal Code: 9431307
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The accurate quantitation of liver **tumor** burden and visualization of lesions in three dimensions (3D) can assist in **treatment** planning and can allow monitoring of therapy. Previous attempts have used CT and standard contrast media. Because the iodinated agents rapidly diffuse into tumors, usually effacing, and at time enhancing **tumor** edges, they decrease accuracy and make image segmentation difficult. CT portography suffers from flow related artifacts and does not allow the distinction of tumors from hemangiomas. Blood pool contrast is ideal in this setting since it enhances liver, liver vessels and hemangiomas, but not tumors, 'physiologically' splitting the image into normal and abnormal tissues. This ongoing study assesses the feasibility of this technique to visualize **tumor** and presents a scheme to automatically quantitate **tumor** volume. It utilized a rabbit VX2 liver **tumor** model and CT scanning shortly after the infusion of 3 ml/kg perflubron emulsion. Cut sections of the frozen carcass served as gross pathologic correlation. Images were imported onto a **Sparc** workstation, 3D reformatted and **tumor** and liver volume calculated. Histograms of pixel intensity clearly separated tumors from liver and liver from surrounding structures allowing the easy demarcation of **tumor** and liver margins.

5/3,AB/24 (Item 24 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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07883562 94022423 PMID: 8105479
Loss of retinoic acid receptor gamma function in F9 cells by gene disruption results in aberrant Hoxa-1 expression and differentiation upon retinoic acid **treatment**.
Boylan J F; Lohnes D; Taneja R; Chambon P; Gudas L J
Department of Pharmacology, Cornell University Medical College, New York,

NY 10021.
Proceedings of the National Academy of Sciences of the United States of America UNITED STATES Oct 15 1993, 90 20 p9601-5, ISSN 0027-8424 Journal Code: 7505876
Contract/Grant No.: 1F32 CA09251-01; CA; NCI; R01CA43796; CA; NCI; R01HD24319; HD; NICHD
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Retinoic acid (RA) signal transduction is believed to be mediated through several high affinity nuclear receptors [RA receptors (RARs) and retinoid X receptors], which are members of the steroid/thyroid/vitamin D superfamily and function as transcription factors. Why multiple RARs exist and what gene targets are regulated by each of the three receptors remain compelling questions in developmental biology. Through targeted disruption of both RAR gamma alleles, we have identified several differentiation-specific genes that are regulated either directly or indirectly by RAR gamma in F9 embryonal carcinoma cells. These include genes encoding Hoxa-1 (Hox-1.6) and the extracellular matrix proteins laminin B1 and collagen type IV (alpha 1), all of which are RA inducible in wild-type F9 embryonal carcinoma cells but are not significantly induced in the RAR gamma-/- lines. In contrast, transcripts encoding Hoxb-1 (Hox-2.9) and cellular RA binding protein II (CRABPII) are activated by RA for a longer period of time in the RAR gamma-/- lines compared to the wild-type F9 line. Not all RA-responsive genes are aberrantly expressed; Rex-1, RAR beta, and **SPARC** transcripts are regulated in the RAR gamma-/- lines as they are in F9 wild-type cells. Our results support the idea that each RAR may regulate different subsets of RA-responsive genes, which may explain, in part, the complex regulation of developmental processes by retinoids.

5/3,AB/25 (Item 25 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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07507293 93031853 PMID: 1412468
Lead inhibits secretion of **osteonectin/SPARC** without significantly altering collagen or Hsp47 production in osteoblast-like ROS 17/2.8 cells.
Sauk J J; Smith T; Silbergeld E K; Fowler B A; Somerman M J
Department of Pathology, University of Maryland Dental School, Baltimore 21201.
Toxicology and applied pharmacology (UNITED STATES) Oct 1992, 116 (2) p240-7, ISSN 0041-008X Journal Code: 0416575
Contract/Grant No.: AF-41572; AF; NIAMS; DE-08648; DE; NIDCR; H75/ATH390067; AT; NCCAM
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
In an effort to better understand the consequences of lead (Pb2+) on skeletal growth, the effects of Pb2+ were investigated using ROS 17/2.8 bone-like cells in vitro. These studies revealed that Pb2+ (4.5 x 10(-6) M -4.5 x 10(-7) M) has little or no effect on cell shape except when added immediately following seeding of the cells. However, proliferation of ROS cells was inhibited, in the absence of serum, at concentrations of 4.5 x 10(-6) M Pb2+. Protein production was generally increased, however, the major structural protein of bone, type I collagen, production was only slightly altered. Following **treatment** of ROS cells with Pb2+, intracellular levels of the calcium-binding protein **osteonectin/SPARC** were increased. **Osteonectin/SPARC** secretion into the media was delayed or inhibited, coincident with retention of **osteonectin/SPARC** there was a decrease in the levels of

osteonectin SPARC mRNA as determined by Northern analysis. These studies suggest that processes associated with **osteonectin SPARC** translation and secretion are sensitive to Pb^{2+}.

5 3/AB 26 Item 26 from file: 155
DIALOG File 155:MEDLINE

07412902 92344875 PMID: 1637573
Immunological screening of **SPARC Osteonectin** in nonmineralized tissues.
Maillard C; Malaval L; Delmas P D
Inserm U234, Hop.tal Edouard Herriot, Lyon, France.
Bone (UNITED STATES) 1992, 13 (3) p257-64, ISSN 8756-3282
Journal Code: 8504048
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

SPARC/Osteonectin is a major bone-related protein that is also present in nonmineralized tissues and in platelets. As compared to bone **SPARC/Osteonectin**, **SPARC/Osteonectin** from platelets presents a slightly lower electrophoretic mobility in SDS-PAGE and a 100-fold decreased affinity for a unique monoclonal antibody, Mab2 (Malaval et al. 1991). To check the tissular diversity of **SPARC/Osteonectin**, protein extracts from bovine bone, nonmineralized tissues, and platelets were screened by immunoblotting and immunoradiometric assay, with Mab2 and three other monoclonal antibodies recognizing distinct epitopes. The **SPARC/Osteonectin** secreted by a human osteosarcoma cell line (MG63) was also tested. In all the nonmineralized tissues tested (gut, bone marrow, tendon, mesentery, artera, lens, skin, liver, and cornea), **SPARC/Osteonectin** presents the same immunoreactivity and electrophoretic mobility as in bone. The heavier molecular weight and Mab2-negative form present in platelets seems to be unique to this cell type. Osteosarcoma cell extracts and conditioned media give the same results as bone extracts, indicating that the low molecular weight and Mab2-positive form of **SPARC/Osteonectin** present in most tissues does not result from proteolytic cleavage in the matrix, but is secreted as such. Bone and platelet **SPARC/Osteonectin** present different patterns of sensitivity to glycosidases, suggestive of a difference in N-glycosylation. However, these **treatments** do not affect the decreased affinity of Mab2 for platelet **SPARC/Osteonectin**, which is not likely to be related to difference in N-glycosylation.

5/3,AB/27 (Item 27 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07390452 92332531 PMID: 1622859
SARG: a new human osteosarcoma cell line. Expression of bone markers and of major histocompatibility antigens.
Scotlandi K; Serra M; Landuzzi L; Baldini N
Laboratorio di Ricerca Oncologica, Istituto Ortopedico Rizzoli, Bologna, Italy.
Annals of oncology : official journal of the European Society for Medical Oncology / ESMO (NETHERLANDS) Apr 1992, 3 Suppl 2 pS29-31, ISSN 0923-7534 Journal Code: 9007735
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

A new cell line SARG was established from a human radiation-induced osteosarcoma OSA . It showed an epithelial-like morphology with polymorphous and sometimes bizarre nuclei. SARG had an osteoblastic differentiation pattern: almost 100% of the cells were positive for alkaline phosphatase, type I and III collagens and **osteonectin**. The expression of class I HLA antigens was detectable even after 40 in vitro passages. The expression of MHC antigens was greatly increased after in vitro **treatment** with interferon-gamma IFN-gamma , whereas interferon-alpha IFN-alpha and **tumor** necrosis factor alpha TNF-alpha increased the expression of class I antigens, but not of class II antigens. SARG was tumorigenic after subcutaneous injection in nude mice. Experimental metastases were never detected.

5 3,AB/28 (Item 28 from file: 155)

07377032 92312344 PMID: 1615759
Identification of proteins secreted by human osteoblastic cells in culture.
Johansen J S; Williamson M K; Rice J S; Price P A
Department of Biology, University of California-San Diego, La Jolla.
Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research (UNITED STATES) May 1992, 7 (5) p501-12, ISSN 0884-0431 Journal Code: 8610640
Contract/Grant No.: AR 27029; AR; NIAMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
To better understand the biochemistry of matrix-forming cells, we developed a simple and reproducible procedure for the isolation and identification by N-terminal sequencing of proteins secreted by cells into culture medium and applied this procedure to the analysis of the major Coomassie blue-staining proteins under 100 kD that are secreted from three different human osteoblastic cell cultures. The major proteins secreted by normal human osteoblasts from adult trabecular bone were identified by N-terminal sequencing to be gelatinase, **osteonectin**, the C-terminal propeptides of the alpha 1 and alpha 2 chains of type I collagen, tissue inhibitor of metalloproteinase 1 (TIMP-1), and beta 2-microglobulin. The amounts of each of these proteins secreted into medium over a 24 h interval did not change over the 7 consecutive days of culture under serum-free conditions, which indicates that this pattern of protein secretion is not significantly affected by the serum-free conditions needed for protein identification by this method. In addition, radioimmunoassay for bone gla protein (BGP), a marker for osteoblast phenotype, revealed that BGP secretion remained high over 7 days of culture under serum-free conditions and was comparable to the rate of BGP secretion in control cultures with 10% serum. The major proteins secreted by MG-63 cells were identified by N-terminal sequencing to be gelatinase, a novel 40 kD human bone protein we termed YKL-40, TIMP-1, the recently discovered TIMP-2, and beta 2-microglobulin. Further studies revealed that YKL-40 is the only protein detectable by Coomassie staining of SDS gels of MG-63 media proteins that is induced by extended time at confluence or by **treatment** with 1,25-(OH)2D3. The apparent absence of detectable Coomassie-stained bands corresponding to the C-terminal propeptides of collagen in the medium of MG-63 cells suggests that these transformed cells may not be a good model for bone matrix formation. The major proteins secreted by normal fetal osteoblastic cells were identified by N-terminal sequencing to be **osteonectin** and the C-terminal propeptides of the alpha 1 and alpha 2 chains of type I collagen. Gelatinase and TIMP could not be detected among the conditioned medium proteins by these methods. These observations indicate that fetal osteoblasts primarily express proteins that are matrix

constituents and adult human osteoblasts secrete, in addition to these, proteins that could function in matrix turnover.

5/3,AB/29 Item 29 from file: 155
DIALOG(R)File 155:MEDLINE(R)
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07307344 92038359 PMID: 1373929
Development and characterization of a rapidly proliferating, well-differentiated cell line derived from normal adult human osteoblast-like cells transfected with SV40 large T antigen.
Keeting P E; Scott R E; Colvard D S; Anderson M A; Oursler M J; Spelsberg T C; Riggs B L
Mayo Graduate School of Medicine, Mayo Clinic, Rochester, Minnesota.
Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research (UNITED STATES) Feb 1992, 7 (2) p127-36, ISSN 0884-0431 Journal Code: 8610640
Contract/Grant No.: AG-04875; AG; NIA; CA-09441; CA; NCI; CA-28240; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
A new bone cell line was established by transfecting normal adult human osteoblast-like (hOB) cells, derived from a 68-year-old woman, with the plasmid pSV3 neo. The plasmid included coding sequences and promoters for the large and small T antigens of the SV40 virus as well as resistance to the antibiotics neomycin and G418. A single antibiotic-resistant colony was located and cloned. Large **tumor** antigen production in the clonal cell line was confirmed by indirect immunofluorescence study. **Treatment** with 1,25-dihydroxy-vitamin D3 increased steady-state concentrations of protein and mRNA for osteocalcin and for alkaline phosphatase. Northern blot analyses also demonstrated the presence of mRNAs for alpha(I)-procollagen, osteopontin 1a, transforming growth factor beta, and interleukin-1 beta. The plasma membrane calcium pump and **osteonectin** were identified by immunocytochemical analysis. These cells produced a matrix that mineralized when beta-glycerophosphate was added to their cultures. As assessed by functional receptor assays, both estrogen and androgen receptors were present and functional, although at low concentrations. **Treatment** with parathyroid hormone did not stimulate adenylate cyclase activity. Thus, these cells are a well-differentiated, steroid-responsive clonal cell line that closely approximates the phenotype of the mature osteoblast. They should serve as an excellent model for the study of osteoblast biology.

5/3,AB/30 (Item 30 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

07219732 92137330 PMID: 1310471
Expression of **SPARC** is correlated with altered morphologies in transfected F9 embryonal carcinoma cells.
Everitt E A; Sage E H
Department of Biological Structure, School of Medicine, University of Washington, Seattle 98195.
Experimental cell research (UNITED STATES) Mar 1992, 199 (1) p134-46, ISSN 0014-4827 Journal Code: 0373226
Contract/Grant No.: 5T32-GM07270; GM; NIGMS; GM-40711; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

SPARC secreted protein, acidic and rich in cysteine is a Ca 2+ binding glycoprotein that has recently been identified as a member of a group of proteins that exert antispreading effects on various cultured cells. In addition, **SPARC** is induced during the later stages of F9 stem cell differentiation to parietal endoderm (PE). When **treated** with retinoic acid and dibutyryl cAMP, F9 cells differentiate into PE and **SPARC** mRNA is increased approximately 20-fold. To determine whether the chronic overexpression or inhibition of expression of **SPARC** would affect the morphology, attachment, or differentiation of F9 cells, we transfected undifferentiated F9 cells with cDNA encoding **SPARC** in anti-sense **SPARC** and cloned lines that expressed either elevated or reduced levels of **SPARC** protein. The transfected F9 cells displayed altered morphologies in culture: cells of four overexpressing lines appeared clumped and rounded, whereas those of three underexpressing lines were spread and flat, in comparison to controls. Moreover, the morphological differences persisted during differentiation of the lines to PE. The altered morphology was not due to an increased expression of collagenases and did not affect the ability of the cells to attach and adhere to tissue culture plastic. The altered phenotype of the transfected F9 cells appeared to be directly related to the level of extracellular **SPARC**. Since overexpression of **SPARC** induced rounding and aggregation of F9 cells in culture, we propose that **SPARC** facilitates modulation of cell-cell or cell-substrate interactions in vivo.

9/3,AB/31 (Item 31 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

07124886 92058109 PMID: 1659122
Retinoic acid modulation of mRNA levels in malignant, nontransformed, and immortalized osteoblasts.
Zhou H; Hammonds R G; Findlay D M; Fuller P J; Martin T J; Ng K W
Department of Medicine, University of Melbourne, Australia.
Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research (UNITED STATES) Jul 1991, 6 (7) p767-77, ISSN 0884-0431 Journal Code: 8610640
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Clonal cell lines presumably "arrested" at a particular stage of differentiation are useful models to study the processes of differentiation in osteoblasts. UMR-201 is a presumptive preosteoblastic nontransformed rat clonal cell line with a limited life span in culture. Two immortalized cell lines, UMR-201-10A (10A) and UMR-201-10B (10B), were derived from UMR-201 by stable transfection with simian virus (SV) 40 large T antigen. This study compares the growth and profile of gene expression of the immortalized cell lines with those of UMR-201 and UMR-106-06, a rat clonal cell line with well-defined osteoblast-like phenotypic characteristics. All four cell lines constitutively expressed the mRNA for the gamma, alpha, and beta receptors for retinoic acid (RA), the growth hormone receptor, pro-alpha 1(I) collagen, **osteonectin**, bone proteoglycan I, and bone morphogenetic proteins (BMP) 1 and 2A. Alkaline phosphatase mRNA was absent in the preosteoblast cell lines but was induced by **treatment** with 10(-6) M RA, which also increased the steady-state levels of mRNA for osteopontin and BMP1. mRNA for matrix gla protein was constitutively present and further induced by RA in UMR-201 and 10B only. Messenger RNA for bone sialoprotein and bone morphogenetic protein 3 were constitutively expressed in UMR 106-06 and UMR-201 but absent in the immortalized cell lines. None of the cell lines expressed measurable mRNA for bone gla protein or bone proteoglycan II. 10B grew more rapidly than UMR-201, but unlike UMR-201, it was also able to proliferate in serum-free medium and exhibit anchorage-independent growth. In summary, this study identifies

novel retinoic acid effects on gene expression in these cells. Differences noted in the expression of mRNAs between UMR-106-06 and the other cell lines may provide some insight into the sequence of expression of these phenotypic characteristics as osteoblasts differentiate.

5/3,AB/32 Item 32 from file: 155
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

06275979 89377594 PMID: 3076861
Isolation of differentially expressed human cDNA clones: similarities between mouse and human embryonal carcinoma cell differentiation.
Wiles M V
Laboratory of Human Molecular Genetics, Imperial Cancer Research Fund, Lincoln's Inn Fields, London, UK.
Development (Cambridge, England) (ENGLAND) Nov 1988, 104 (3) p403-13
, ISSN 0950-1991 Journal Code: 8701744
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The study of early human development is of great importance but has been limited by the lack of suitable reagents. Recently, however, the human embryonal carcinoma (EC) cell line NT2D1 has been isolated. This cell line will differentiate upon exposure to retinoic acid (RA). A cDNA library was constructed from poly(A)+ RNA derived from NT2D1 cells **treated** with 10(-6) M-RA for 7 days (delta NT2D1 cells). By differential cDNA screening, it was found that 1.12% of delta NT2D1 cDNA recombinants screened detected an increase in signal with 32P-cDNAs derived from delta NT2D1 as compared with NT2D1. To compare RA-induced differentiation of mouse and human EC cells, the delta NT2D1 cDNA library was rescreened with 32P-cDNAs derived from the mouse EC cell line F9 and the result compared with 32P-cDNA derived from F9 differentiated to parietalendoderm (F9PE)-like cells and visceral-endoderm (F9VE)-like cells. Approximately 1.2% of the delta NT2D1 cDNA recombinants detected a differential increase in signal following differentiation of mouse EC cells to F9VE and/or F9PE. Of these homologous regulated sequences, 0.3% were common to both mouse and human EC cell RA-induced differentiation. Five different cDNA clones were isolated that detect a marked increase (5- to 75-fold) in mRNA abundance following RA-induced differentiation of NT2D1. Of these five clones, three detect homologous mRNAs which also increase in abundance following differentiation of the mouse EC cell line F9 to PE- and/or VE-like cells; the other two clones do not detect sequences in the mouse mRNAs tested. One clone shows homology to **SPARC** , a gene known to be regulated during mouse embryonic development. While another clone, 305A, has a limited range of expression, being detected in F9VE and in a human parietal-endoderm-like cell, but not in F9PE and a human visceral-endoderm-like cell. This work shows that there are both similarities and differences in mouse and human EC cell differentiation, and these cDNA clones provide some of the first reagents for studying the molecular biology of human development.

5/3,AB/33 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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13853097 BIOSIS NO.: 200200482118
High pressure effects on cellular expression profile and mRNA stability. A cDNA array analysis.
AUTHOR: Sironen Reijo K; Karjalainen Hannu M; Torronen Kari; Elo Mika A; Kaarniranta Kai; Takigawa Masaharu; Helminen Heikki J; Lammi Mikko J*a
AUTHOR ADDRESS: a-Department of Anatomy, University of Kuopio, 70211, P.O. Box 1627, Kuopio**Finland E-Mail: mikko.lammi@uku.fi

JOURNAL: Biorheology 39 1-2 :p111-117 2002
MEDIUM: print
ISSN: 0006-355X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Hydrostatic pressure has a profound effect on cartilage tissue and chondrocyte metabolism. Depending on the type and magnitude of pressure various responses can occur in the cells. The mechanisms of mechanotransduction at cellular level and the events leading to specific changes in gene expression are still poorly understood. We have previously shown that induction of stress response in immortalized chondrocytes exposed to high static hydrostatic pressure increases the stability of heat shock protein 70 mRNA. In this study, our aim was to examine the effect of high pressure on gene expression profile and to study whether stabilization of mRNA molecules is a general phenomenon under this condition. For this purpose a cDNA array analysis was used to compare mRNA expression profile in pressurized vs. non-pressurized human chondrosarcoma cells (HCS 2/8). mRNA stability was analyzed using actinomycin-**treated** and nontreated samples collected after pressure **treatment**. A number of immediate-early genes, and genes regulating cell cycle and growth were up-regulated due to high pressure. Decrease in **osteonectin**, fibronectin, and collagen types VI and XVI mRNAs was observed. Also bikunin, rdc37 homologue and Tiam 1, genes linked with hyaluronan metabolism, were down-regulated. In general, stability of down-regulated mRNA species appeared to increase. However, no increase in mRNA above control level due to stabilization was noticed in the genes available in the array. On the other hand, mRNAs of certain immediate-early genes, like c-jun, jun-B and c-myc, became destabilized under pressure **treatment**. Increased accumulation of mRNA on account of stabilization under high pressure conditions seems to be a tightly regulated, specific phenomenon.

2002

5/3,AB/34 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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13780497 BIOSIS NO.: 200200409318
A novel tissue-specific and **tumor**-restrictive human **osteonectin** promoter-mediated gene therapy for **treatment** of androgen-independent human prostate **cancer**.
AUTHOR: Hsieh Chia-Ling(a); Zhau Haiyen E(a); Chung Leland W K(a)
AUTHOR ADDRESS: (a)Department of Urology, Molecular Urology and Therapeutic Program, Emory University School of Medicine, Atlanta, GA**USA
JOURNAL: Proceedings of the American Association for Cancer Research Annual Meeting 43p800-801 March, 2002
MEDIUM: print
CONFERENCE/MEETING: 93rd Annual Meeting of the American Association for Cancer Research San Francisco, California, USA April 06-10, 2002
ISSN: 0197-016X
RECORD TYPE: Citation
LANGUAGE: English
2002

5/3,AB/35 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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13589067 BIOSIS NO.: 200200217888

The diagnostic value of immunohistochemical detection of **osteonectin** in different types of osteosarcoma.
AUTHOR: Shaban Amal A a
AUTHOR ADDRESS: a Pathology Department, Faculty of Medicine, Alexandria University, Alexandria**Egypt
JOURNAL: Journal of the Medical Research Institute 22 3 :p134-150 2001
MEDIUM: print
ISSN: 1110 0133
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The pathologic diagnosis of osteosarcoma may be problematic due to wide histopathologic variations that can be mimicked by other primary or metastatic bone tumors with significantly different biologic potentials and **treatment** protocols. The accurate diagnosis of osteosarcoma relies on identification of malignant osteoblasts that are capable of producing neoplastic osteoid or bone matrix. To determine the benefit of immunohistochemistry for the diagnosis of osteosarcoma, twenty five cases of various types of osteosarcoma, seven fine needle aspirate of osteoblastic osteosarcoma, and eleven control lesions of nonosteogenic bone tumors were immunostained with monoclonal antibodies for **osteonectin** (a 32 Kda non collagenous bone protein). The production of **osteonectin** depends on the osteoblast-like function of the individual **tumor** cells, therefore, a homogenous immunocytochemical staining of all **tumor** cells and the surrounding matrix cannot be expected. Nevertheless, all cases of osteosarcoma demonstrated positive cell cytoplasmic and matrix staining with variable intensities. All control cases-except one case of conventional chondrosarcoma-showed negative cell cytoplasmic and matrix staining. In conclusion, immunohistochemical demonstration of **osteonectin** in osteosarcomas is a valuable tool for establishment of their osteogenic origin in order to differentiate them from other nonosteogenic bone tumors. The technique is reproducible in fine needle aspirates of osteosarcoma, which is considered as a noninvasive and easy diagnostic procedure.

2001

5/3,AB/36 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

13039309 BIOSIS NO.: 200100246458
Stroma-epithelial interaction in prostate **cancer** as the basis for molecular co-targeting with adenoviral vectors.
AUTHOR: Chung Leland W K(a); Law Andy(a); Hsieh Chia-Ling(a); Matsubara Shigeji(a); Rhee Hong(a)
AUTHOR ADDRESS: (a)U. Virginia Health Sciences Center, University of Virginia, Charlottesville, VA, 22908**USA
JOURNAL: FASEB Journal 15 (4):pA239 March 7, 2001
MEDIUM: print
CONFERENCE/MEETING: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Reciprocal cell interaction between prostate **cancer** and bone or prostate stromal cells demonstrated the importance of **tumor** and microenvironment interaction, which regulates local **tumor** growth, and its acquisition of androgen-independence and metastatic

potential. This study documented that prostate **cancer** and bone or prostate stromal cells when co-cultured under 3-D microgravity stimulated growth conditions underwent non-random permanent phenotypic and genotypic changes in both **tumor** epithelial and bone stromal cellular compartments. These results support the role of cellular interaction and prostate carcinogenesis. Using lineage-derived LNCaP cell lines as a model for the evaluation of multi-step prostate carcinogenesis, we observed that prostate **cancer** cells that have acquired the ability to metastasize to the skeleton exhibit osteomimetic properties. By employing this cellular interaction model, we have developed a series of tissue-specific and **tumor**-restrictive promoters, osteocalcin, bone sialoprotein, and **osteonectin**, which have a unique ability to target prostate **cancer** and prostate and bone stromal cells in tumors. This strategy of co-targeting has been applied in both pre-clinical and/or clinical settings. We have constructed and tested replication-defective adenoviruses to **treat** both localized and metastatic prostate cancers. This strategy is being expanded presently to the use of replication competent adenoviral vectors for the **treatment** of prostate **cancer** skeletal metastasis.

2001

5/3,AB/37 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10291110 BIOSIS NO.: 199698746028
Comparative expression of the **SPARC** and stromelysin-3 genes in mammary tumours.
AUTHOR: Podhajcer O L; Wolf C; Lefebvre O; Segain J-P; Rouyer N; Stoll I; Rio M-C; Chambon P; Basset P(a)
AUTHOR ADDRESS: (a)Inst. Genet. Biol. Mol. Cell., CNRS/INSERM/ULP/Coll. France, BP 163, 67404 Illkirch Cedex, CU de**France
JOURNAL: Breast 5 (1):p13-20 1996
ISSN: 0960-9776
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: By differential screening of a human breast **cancer** cDNA library, we have isolated a cDNA which encodes **SPARC** (**osteonectin**/BM40), a secreted glycoprotein which modulates cell-matrix interactions. The **SPARC** gene was found to be expressed in all invasive human breast carcinomas, metastatic lymph nodes and mouse mammary turnouts that were examined. In these tumours **SPARC** transcripts were specifically detected in fibroblastic cells in the stroma surrounding **cancer** cell islands. In human carcinomas, but not in mouse mammary turnouts, a subset of cells expressing the **SPARC** gene also expressed the stromelysin-3 gene, which encodes a matrix metalloproteinase. These observations support the concept that the stromal component of human breast carcinomas is a major source of extracellular proteins and may be involved in the modulation of tumour progression. Future approaches to **cancer treatment** should include attempts to interfere with the formation and/or functioning of tumour stroma.

1996